Topics in Gastroenterology

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edited by
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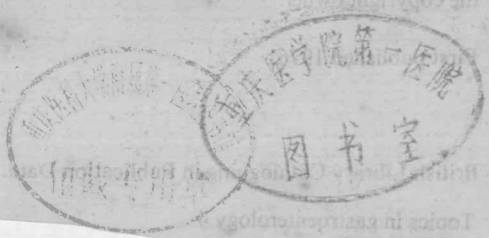

BLACKWELL SCIENTIFIC PUBLICATIONS

OXFORD LONDON EDINBURGH MELBOURNE

Osney Mead, Oxford, OX2 0EL
8 John Street, London, WC1N 2HY
9 Forrest Road, Edinburgh, EH1 2QH
P.O. Box 9, North Balwyn, Victoria, Australia.

First published 1976

British Library Cataloguing in Publication Data.

Topics in gastroenterology 4
Bibl.—Index
ISBN 0-632-00229-8
1. Truelove, Sidney Charles 2. Ritchie, James Alan
616.3 RC801
Digestive organs—Diseases

Distributed in the United States of America by
J.B. Lippincott Company, Philadelphia

and in Canada by
J.B. Lippincott Company of Canada Ltd, Toronto.

Printed and bound in Great Britain
at the Alden Press, Oxford

Preface

Once again, we are presenting a book which is based on the annual Oxford course in postgraduate gastroenterology. The chapters are a written version of the lectures given in the course and it is a great pleasure to thank our contributors for them. We also wish to thank Mrs Zena Jennings for her invaluable assistance in organizing the course and in assembling the material for publication.

We are grateful to our publishers, Blackwell Scientific Publications, with whom it is always a pleasure to work. In particular we wish to thank Mr Per Saugman, their Chairman and Managing Director, for his active support.

We are happy to acknowledge the enthusiastic co-operation we have received from Mr John Robson, their Production Director, and from his assistant, Mrs Diana Porter.

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Chapter 1
Clinical aspects of viral hepatitis

JOAN TROWELL

For many centuries contagious jaundice has caused epidemics; these have been particularly associated with military campaigns and civil disorder. The first recorded epidemic following parenteral transmission of the virus occurred in Bremen, Germany, in 1883 when 1289 shipyard workers were vaccinated against smallpox with lymph obtained from the vesicles of other vaccinated patients and 191 developed jaundice (Lürman, 1885). Since then the parenteral transmission of hepatitis has been associated with many situations in which needles, syringes and other instruments are contaminated with blood or serum. Hepatitis may follow blood transfusion or injection of blood products. Vaccines carry a risk of hepatitis if blood or serum is used in their manufacture (Table 1.1).

Table 1.1. Circumstances favouring the transmission of hepatitis virus

Faecal–Oral	Parenteral
Wars	Injections
Institutions	Blood transfusion
Contaminated food	Exposure to blood products
Contaminated water	Drug addicts
Occupational risk	Tattooing
	Dental treatment
	Renal dialysis

Hepatitis A and B

Although many names were given to the jaundice following parenteral transmission of hepatitis, it was recognized that this was a viral

hepatitis, and it was referred to as serum hepatitis, or hepatitis B, in contrast to infectious hepatitis (hepatitis A). Both hepatitis A and hepatitis B may be acquired orally or parenterally (Krugman *et al*, 1967), but hepatitis A is the more contagious and is usually responsible for epidemics of hepatitis in the community and in institutions. However, Krugman and his colleagues found both hepatitis A and B to be endemic in Willowbrook State School for mentally retarded children in New York. Their studies showed that the two forms of hepatitis could be distinguished by the length of the incubation period, between 31 and 38 days for hepatitis A, and from 41 to 69 days for hepatitis B. After the discovery of Australia antigen (Blumberg *et al*, 1965, 1968) the Willowbrook studies showed that this was present in the serum of patients with hepatitis B during the incubation period and during the early part of the clinical illness. The short incubation period hepatitis (hepatitis A) was not associated with Australia antigen at any stage of the infection. Australia antigen is now termed HB_sAg (Chapter 2).

It may be difficult in an individual patient to establish if an illness is due to infection with hepatitis virus A or virus B. The finding of HB_sAg in the serum will establish that it is hepatitis B but, as this is often a transient finding early in the illness, the patient may have been seen too late in the illness for the antigen to be detected (Fig. 1.1).

In some patients it is possible to estimate the length of the incubation period. There may be a history of contact with another jaundiced patient, or of an event, such as blood transfusion, that could have facilitated parenteral transmission of the virus. When this occurs the length of incubation period may allow a firm diagnosis to be made. However, even then there is sometimes confusion; in epidemics the incubation period of hepatitis appears remarkably constant (Pickles, 1939) but sporadic cases show considerable overlap in the incubation periods of hepatitis A and B. While this may be due to variations in the virus, or even to the presence of more than two viruses causing hepatitis, it may also be due to variations in the immunity of the patients and to the route of infection. This was shown experimentally by the studies at Willowbrook School where serum which was known to cause hepatitis B was given intramuscularly or orally. Incubation periods were considerably shorter when the infecting dose was given as an intramuscular injection (Giles *et al*, 1969).

There are other reasons why in practice the length of the incubation period is of limited value in distinguishing between

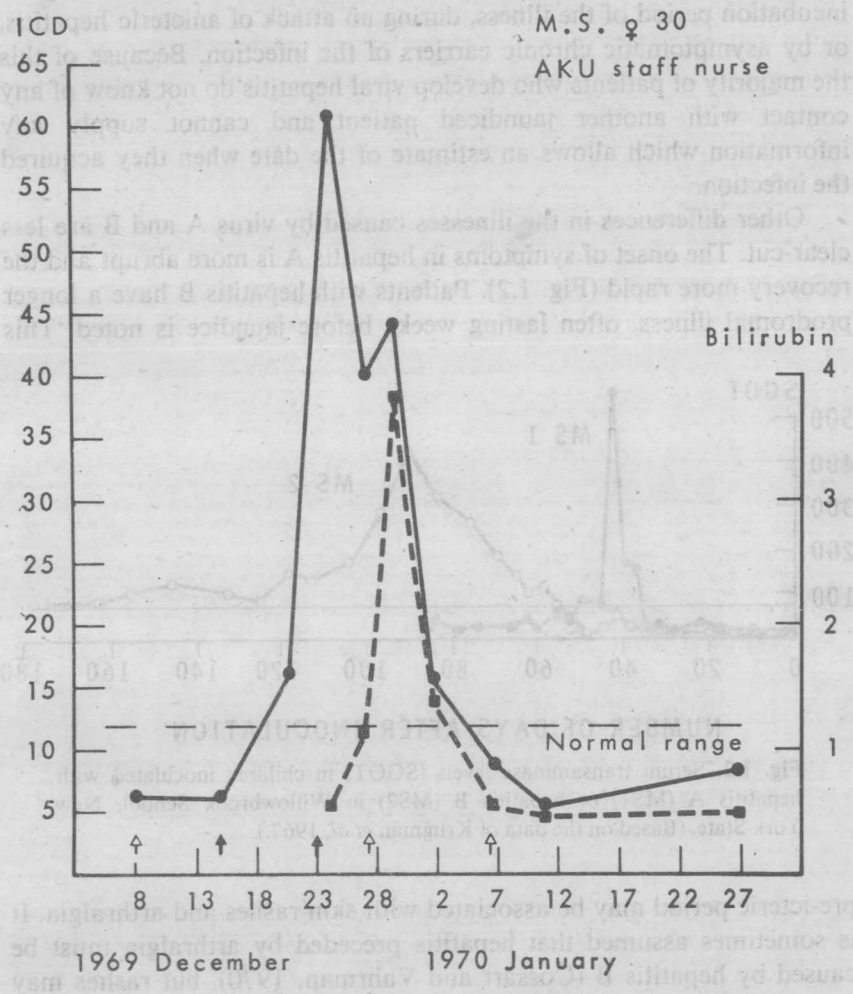

Fig. 1.1. The results of liver function tests and the detection of HB_sAg in the serum of a patient with hepatitis B. Solid Line (●——●) Isocitric dehydrogenase (ICD) mg/100 ml. Dotted Line (■----■) Bilirubin mg/100 ml. ⇧ HB_sAg not detected by electron microscopy. ↑ HB_sAg detected by electron microscopy. The patient was a staff nurse on a renal dialysis unit in which there was weekly screening for hepatitis. HB_sAg and Dane particles were detected on 15 December before any symptoms were present and before serum enzyme levels rose. HB_sAg would not have been found if this patient's serum had not been checked until she was jaundiced.

hepatitis A and B. The infection may be spread by patients during the incubation period of the illness, during an attack of anicteric hepatitis, or by asymptomatic chronic carriers of the infection. Because of this the majority of patients who develop viral hepatitis do not know of any contact with another jaundiced patient and cannot supply any information which allows an estimate of the date when they acquired the infection.

Other differences in the illnesses caused by virus A and B are less clear-cut. The onset of symptoms in hepatitis A is more abrupt and the recovery more rapid (Fig. 1.2). Patients with hepatitis B have a longer prodromal illness, often lasting weeks before jaundice is noted. This

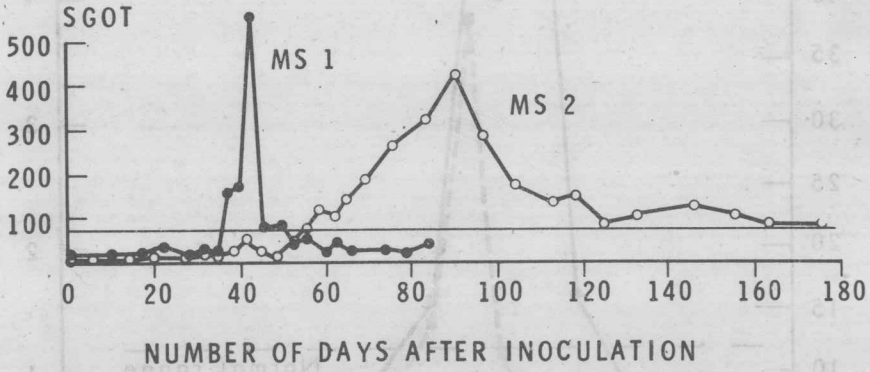

Fig. 1.2. Serum transaminase levels (SGOT) in children inoculated with hepatitis A (MS1) or hepatitis B (MS2) in Willowbrook School, New York State. (Based on the data of Krugman *et al*, 1967.)

pre-icteric period may be associated with skin rashes and arthralgia. It is sometimes assumed that hepatitis preceded by arthralgia must be caused by hepatitis B (Cossart and Vahrman, 1970), but rashes may occur in epidemics of hepatitis which are presumed to be due to hepatitis A from the short incubation period and the absence of HB_sAg.

Clinical picture

Acute hepatitis

Although the time scale of the illness varies in infection with virus A or B, the clinical picture is very similar.

The incubation period is usually symptom free but occasionally a

patient describes one or more days when he was unwell with lethargy and vomiting, and in retrospect often compares these episodes with the symptoms of the prodromal period. HB_sAg and the Dane particles which are assumed to be the hepatitis B virus (Dane *et al*, 1970) have been detected in the serum of patients towards the end of the incubation period of hepatitis B.

The prodromal phase of the illness is the 5 or more days before the patient becomes jaundiced when there is symptomatic and biochemical evidence of hepatic necrosis. This causes acute illness, with lethargy and anorexia and often with vomiting and abdominal pain. The severity of symptoms varies widely. The pain may be only a slight discomfort in the right hypochondrium but sometimes it is more severe. If it is the most distressing symptom, the patient may be admitted to a surgical ward. The patient may be febrile and may have rigors. The fever, rigors and abdominal pain preceding the jaundice make it impossible to distinguish clinically between a viral hepatitis and a cholangitis.

Infection with either hepatitis virus may cause an anicteric or an icteric illness. As most cases of anicteric hepatitis are not diagnosed, it is difficult to establish its incidence. In epidemics of hepatitis the number of patients with anicteric illness exceeds the number who become jaundiced. When ninety-seven players and coaches of a college football team were exposed to contaminated drinking water thirty-two of these men become jaundiced between 4 and 5 weeks later. However, sera from fifty-eight men who were not jaundiced showed elevated serum enzyme values (Chang and O'Brien, 1970).

The severity of a patient's symptoms often lessens soon after he becomes jaundiced. This is most striking in infection with hepatitis virus A. However, a minority of patients develop a cholestatic illness with prolonged jaundice and itching of the skin. A patient who is seen at this stage of the illness presents a clinical picture indistinguishable from that produced by an obstruction of the large bile ducts.

Most patients with hepatitis lose weight, commonly between 5 and 10 kg, but with a severe and protracted attack even more may be lost. Rarely a patient with a severe prolonged illness may develop oedema and ascites, but this does not preclude eventual complete recovery.

Convalescence from hepatitis may be prolonged. Patients often experience minor episodes of nausea and malaise which may recur over 6 months or more after the initial attack. Depression also occurs, but this only rarely requires specific therapy. These 'post-hepatitis'

symptoms may occur without any objective evidence of continuing illness. If the liver function tests remain normal, the patient may be reassured that complete recovery is to be expected. A proportion of patients do have a relapse with a recurrence of the symptoms, signs and abnormal liver function tests about 1 to 2 months after the first illness. The majority of these patients also recover uneventfully.

In most patients the illness, although unpleasant, is benign and recovery appears to be complete. In a small number, the illness may progress to acute liver failure (Fig. 1.3). Patients with hepatitis and hepatic coma have a poor prognosis. The risk of death increases with

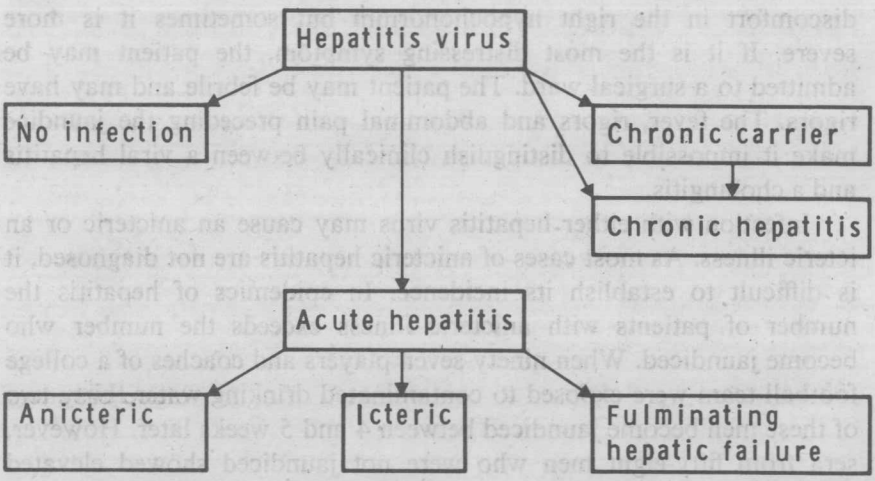

Fig. 1.3. The range of illness which follows infection with hepatitis B (see also Fig. 1.4).

the age of the patient, but probably under 20% of all patients with acute liver failure survive. Because of the large number of patients with anicteric hepatitis, the mortality rate of viral hepatitis is not known, but it has been estimated as of the order of 1 per 1000.

Liver function tests in hepatitis

The acute liver-cell damage which occurs in the prodromal period is accompanied by a sharp rise in the levels of serum enzymes, of which the serum transaminases (SGOT, SGPT, AST) are the most commonly measured. An increase in the levels of these serum enzymes is not specific for viral hepatitis, but liver damage due to hepatitis virus